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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,701	11/30/2001	Henry Yue	PF-0631-2 DIV	5300

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,701	YUE ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 5 26 04.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,2,11,30-45,56,57 and 60-62 is/are pending in the application.

4a) Of the above claim(s) 1,2,56 and 57 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 11,30-45 and 60-62 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of U.S. Application Serial Number 09/470,946, which is a divisional of U.S. Application Serial Number 09/187,331.

Claims 3-10, 12-29, 46-55 and 58-59 have been canceled.

New claims 60-62 have been added.

Claims 1, 2, 11, 30-45, 56, 57 and 60-62 are currently pending.

Election/Restrictions

1. Claims 1, 2, 56 and 57 stand as being withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 13, 2003.

In view of Applicant's amendment filed May 26, 2004 the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 30, 33 and 35 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It was previously stated: "The claims are drawn to diagnostic tests for conditions or diseases associated with the expression of SEQ ID NO: 1 using antibodies to SEQ ID NO: 1. The specification asserts that the discovery of new cell surface glycoproteins satisfies a need in the art by providing new compositions that are useful in the diagnosis, prevention, and treatment of hematologic, karyotypic, and neuronal disorders (page 3, lines 10-12 for example). However, the application does not identify a single disease condition where the expression of SEQ ID NO: 1 or a biological activity of SEQ ID NO: 1 may be a relevant factor or useful for the diagnosis of that disorder.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. However, the specification discloses only two examples of a polypeptide that is naturally-occurring and has at least 90% identity to SEQ ID NO: 1; namely, the polypeptide of SEQ ID NO:1 and the PBDX

protein taught by Ellis et al. (Nature Genetics [1994] 6:394-400; 2 on form PTO-1449) , later identified as the blood group antigen Xg^a Ellis (Nature Genetics [1994] 8:285-290; 3 on form PTO-1449), which is 92.3% identical to SEQ ID NO: 1. However, even a function for Xg^a has not been identified. Ellis (Nature Genetics [1994] 8:285-290; 3 on form PTO-1449) discloses that Xg^a is 48% homologous, including conservative changes, to CD99 and concludes that Xg^a and CD99 are structurally related and therefore "may have a similar function." However, Ellis goes on to say that although CD99 is expressed abundantly on hematopoietic precursor cells and high levels of CD99 constitute a tumor marker for Ewing's sarcoma, "The exact biological function of CD99 is still obscure" (paragraph bridging pages 288-289 in particular). Ellis further discloses that expression of Xg^a is correlated with the exprcssion of CD99. However, while the expression of CD99 has been tied to a particular type of sarcoma, no such correlation has been identified for Xg^a (Ellis - Nature Genetics [1994] 8:285-290; Table 3 in particular). Accordingly, since the identification of SEQ ID NO: 1 as a cell surface marker protein relies solely on it's "significant" identity with Xg^a, not on an actual elucidation of diseases or conditions in which SEQ ID NO: 1 expression or activity is relevant, diagnosis of any condition or disease based upon the expression of SEQ ID NO: 1 is not enabled. Based upon the paucity of guidance from the instant specification and the lack of predictability based upon the state of the art at the time the invention was made, the artisan would not be able to practice the claimed method of diagnosing a condition or disease related to expression of SEQ ID NO: 1 because the artisan would not be able to identify even a single related condition or disease. Therefore, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue with respect to other diagnosing a condition or disease related to expression of SEQ ID NO: 1.

In view of the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would takc undue trials and crrors to practice the claimed invention and the statute does not sanction this."

Applicant's arguments filed May 26, 2004 have been fully considered but they are not persuasive. Applicant argues that the claims are enabled because "[o]ne of skill in the art would know which diseases or disorders are associated with the expression of a cell surface glycoprotein and, therefore, the claimed antibodies which bind the cell surface glycoprotein" (page 8 of response). However, different cell surface glycoproteins are associated with different cell types and expression of different cell surface glycoproteins on the surface of those cells can be altered based upon the presence or absence of a particular disease or disorder. The subgenus of "hematologic, karyotypic, and neuronal disorders" asserted by Applicant itself has three unrelated subgenera that encompass a large number of diseases or disorders that are again are associated with different cell types and with the expression of different cell surface glycoproteins on the surface of those cells that can be altered based upon the presence or absence of a particular disease or disorder. Applicant's claims are drawn to the identification of the cell surface glycoprotein with the primary peptide sequence of SEQ ID NO: 1, which Applicant asserts is a novel, i.e., not previously known sequence. Accordingly, one of skill in the art would have no way of knowing what diseases or disorders the cell surface glycoprotein with the primary peptide sequence of SEQ ID NO: 1 would be associatcd with prior to the disclosurc of SEQ ID NO: 1 by Applicant in the instant

specification. Accordingly, the artisan would have no way of knowing what conditions to diagnose because no conditions are disclosed in the instant specification.

3. Claims 11, 30-45 and 60-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It was previously stated: "The claims recite as part of the invention an antibody which specifically binds a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1" and to a "biologically active fragment" of the polypeptide of SEQ ID NO: 1.

A polypeptide comprising the amino acid sequence of SEQ ID NO: 1 is adequately described in the specification as-filed, thereby providing an adequate written description of an antibody which specifically binds the polypeptide of SEQ ID NO:1 or immunogenic fragments thereof.

A polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" is a recitation of a genus of polypeptides for which Applicant has disclosed only two species: the polypeptide of SEQ ID NO:1 and the XG protein taught by Ellis et al. (Nature Genetics [1994] 8:285-290; 3 on form PTO-1449), which is 92.3% identical to SEQ ID NO: 1. The sequence recited in claim 1 of SEQ ID NO: 1 is 195 amino acid residues in length. Assuming that the 90% identical peptides are limited to a similar length of 195 amino acids and using only the 20 naturally occurring amino acid residues, the claim includes all peptides that have up to 19 amino acid changes, resulting in a genus encompassing more than 3.76×10^{25} (19^{20}) different polypeptides. However, Applicant does not appear to have provided a description of which polypeptide sequences are "naturally-occurring", even among those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 1.

Neither does Applicant appear to have provided a description of a biological activity of SEQ ID NO: 1 or fragments thereof, even for those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 1. As stated supra, the identification of SEQ ID NO: 1 is based upon its "significant" identity to the XG protein taught by Ellis. However, even Ellis has not identified a function for XG. Ellis (Nature Genetics [1994] 8:285-290; 3 on form PTO-1449) discloses that XG is 48% homologous, including conservative changes, to CD99 and concludes that XG and CD99 are structurally related and therefore "may have a similar function." However, Ellis goes on to say that although CD99 is expressed abundantly on hematopoietic precursor cells and high levels of CD99 constitute a tumor marker for Ewing's sarcoma, "The exact biological function of CD99 is still obscure" (paragraph bridging pages 288-289 in particular). Thus neither the common attributes of the genus nor the identifying attributes of individual species other than SEQ ID NO: 1 appear to have been described.

One of skill in the art would conclude that Applicant was not in possession of the claimed genera of polypeptides comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" and "biologically active fragments of a polypeptide having the amino acid sequence of SEQ ID NO: 1." Since Applicant does not appear to have been in possession of the genus of polypeptides to which the instantly recited antibody specifically binds; Applicant in turn does not appear to be in possession of the genus of antibodies specifically binding these polypeptides.

Therefore, only an antibody to SEQ ID NO: 1 or immunogenic fragments thereof meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the

filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398."

Applicant argues that the specification sufficicntly describes the function of the claimed polypeptides because SEQ ID NO: 1 shares 92.3% identity with the PBDX protein taught by Ellis (of record) and therefore would "be expected to have a similar function as a XG blood group system marker" (pages 9-10 of the response). However, Ellis teaches that is structurally related (48% homologous) to, and may have a similar function to, CD99 and that the "exact biological function of CD99 is still obscure" (paragraph bridging pages 288-289 in particular). Therefore, Applicant's allegation of known function of the polypeptide of SEQ ID NO: 1 is based upon 92.3% identity to a polypeptide that is 48% homologous to (and may have a similar function to) a protein whose biological function is itself not known. The facts of the matter do not, therefore, support Applicant's assertion that the specification sufficiently desribes the function of the disclosed polypeptides to which antibodies are claimed.

Applicant further argues that there is adequate written descriptive support for variants sharing at least 90% (claim amended to recite 95%) identity to SEQ ID NO: 1 and therefore adequately describes the claimed antibodies thereto. Applicant contends that "[a] variant that is al least 90% identical to a sequence of known function is highly likely to share the same function" on page 10 of the response. However, as stated above, the function of SEQ ID NO: 1 has not been established because the functional assertion is based upon ultimate homology to a known polypeptide whose own biological function is itself obscure. Furthermore, as stated previously, the claim reads upon a genus of which exactly 2 species are known. However, the genus encompasses over 3.76×10^{25} (19^{20}) different polypeptides at 90%. At 95%, the genus encompasses over 6.02×10^{19} different species with only a single species described (SEQ ID NO: 1). This can hardly be considered adequate written descriptive support.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 11, 31, 32, 34, 36-43 and 60-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Ellis et al. (Nature Genetics [1994] 8:285-290; 3 on form PTO-1449).

It was previously stated: "Ellis teaches the making of polyclonal rabbit and monoclonal murine antibodies to PBDX by immunizing animals with the immunogenic N-terminal peptide (not including the leader sequence) QRDFDLADALDDP with a C-terminal cysteine residue attached to cross-link the peptide to a thyroglobulin carrier (paragraph bridging pages 285-286 and page 289, first column in particular). Ellis teaches that the antibodies bind to PBDX protein and identify it as the naturally-occurring Xg^a blood group antigen (Abstract in particular). The prior art teaching anticipates the claimed invention.

Claims 42 and 43 are included because the claims are drawn to a specific product and are drafted in a product-by-process manner. The patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim (see *In re* Thorpe, 227 USPQ 964 (Fed. Cir. 1985))."

Applicant asserts that the PBDX protein taught by Ellis is only 92.3% identical and the claims have been amended to recite that the peptide is at least 95% identical to SEQ ID NO: 1. Applicant argues, therefore, that Ellis cannot be considered to be anticipatory because the PBDX polypeptide is outside the scope of the claim. However, it is noted that the antibodies of Ellis were made using an immunogenic fragment of PBDX having the amino acid sequence "QRDFDLADALDDP." The immunogenic peptide of Ellis is identical to amino acid residues 22-34 of SEQ ID NO: 1. Accordingly, the antibodies of Ellis will bind to SEQ ID NO: 1, irrespective of the level of identity in the remainder of the polypeptide.

Conclusion

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
August 2, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
8/4/02